UNITED STATES DEPARTMENT OF COMMERCE
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VB

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 08/905,709 | 08/05/97 | STERN D | 52876/JPW/JM |

HM12/0615

COOPER & DUNHAM
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| EXAMINER | |
|---|---|
| LAZAR WESLEY,E | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | 14 |

**DATE MAILED:** 06/15/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

## Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 08/905,709 | Stern |
| **Examiner** | **Group Art Unit** |
| Eliane Lazar-Wesley | 1642 |

☐ Responsive to communication(s) filed on _____.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) *1-10, 12-27, and 29-35* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-10, 12-27, and 29-35* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

*--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---*

## DETAILED ACTION

### *Continued Prosecution Application*

1. The request filed on March 23, 2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/905,709 is acceptable and a CPA has been established. An action on the CPA follows.

Claims 1-10, 12-27 and 29-35 are under consideration.

### *Claim Objections*

2. In claim 19, line 2, the word "a" is missing between "of" and "macrovessel".

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 12-27 and 29-35 remain rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement "to prevent accelerated development of atherosclerosis in a subject predisposed thereto", or "to inhibit progression of macrovessel disease in a subject predisposed thereto". The specification discloses an example of treatment (page 32, line 33+) of artificially induced diabetic knockout mice (that are apolipoprotein E deficient, page 31,

lines 9-12) with sRAGE, the treatment being started two weeks after induction of diabetes and continuing for 6 weeks, and discloses, page 34, line 25+, that in these artificially induced diabetic mice , atherosclerotic plaques at the major branches of the aortic tree and at the arch of the aorta were markedly diminished in the mice treated with sRAGE (Figure 3). However, the specification is not enabled for a method of prevention of accelerated development of atherosclerosis or inhibition of progression of a macrovessel disease. The example provided refers to a case of artificially induced diabetes in apolipoprotein E deficient mice, where the time of start of the disease is clearly known, where the evolution of the disease is monitored, and where intervention is practiced at an early stage, like possibly a stage where the AGEs are not "sticking" to the cell walls and wherein a soluble form of RAGE can possibly "trap" the AGEs. Atherosclerosis and macrovessel diseases are usually diseases that develop over an extended period of time, that do not show symptoms for long periods of time, and for which the "starting point" is unknown. Even if numerous risk factors for atherosclerosis have been cited in the medical and scientific literature , there is no clear parameter defining who is predisposed to develop it, at which stage of their life, under which circumstances, and how and when the polypeptide should be administered. The susceptibility to atherosclerosis and macrovessel disease varies greatly among individuals exposed to identical risk factors, and it is unpredictable which individual is going to develop the disease and over which period of time. The specification does not provide guidance about how to determine who is predisposed to develop the diseases or at which stage of the disease the polypeptide should be administered. It is unpredictable if the prevention will work in an established or an advanced stage of disease, in a case of naturally

occurring diabetes in human for example, or in which type of diabetes (juvenile or late onset diabetes, diabetes type I or II) . It is unpredictable when to provide the treatment, and for how long, and if the effect of the treatment is long term or wears off after a while. It is even less predictable if the prevention method would work in other diseases where atherosclerosis and macrovessel disease are not associated specifically with diabetes, like different types of hyperlipidemia or hypothyroidism. In view of the lack of guidance and working example, considering the state of the art and that it is unpredictable who is predisposed to develop the disease and when the preventive treatment should be applied, it would constitute undue experimentation to make and/or use the invention commensurate in scope with the claims.

Applicants's arguments have been considered, but are not found persuasive for the reasons discussed above and the following ones. Applicants argue that the specification gives a full description of clinical signs, biochemical signs and hereditary disorders which would indicate that a person is predisposed to accelerated atherosclerosis. While the Examiner agrees that numerous risk factors are known (like high blood pressure, obesity) and may play a role in the development of vascular diseases, it is still unpredictable to determine who is predisposed to develop the vascular diseases (like for example which person drinking soft as opposed to hard water), and who would be prevented from accelerated development of atherosclerosis, at which stage of the disease, under which conditions, through the administration of a soluble receptor for advanced glycation product, or a derivative thereof that inhibits the interaction of AGE and RAGE . Further, the model system used

(artificially induced diabetes in knockout mice ) is not predictive of prevention in such patients, for reasons cited above.

The amendments to claims 1 and 19 do not obviate the rejections, because it is still unpredictable to which population of patients , at which stage of the disease, for which specific type of disease (which macrovessel disease, for example) the method should apply, and in view of the state of the art, it would constitute undue experiment to practice the invention commensurate in scope with the claims.

Claims 1 and 19 remain rejected under 35 USC 112, first paragraph, for the reasons of record in the former Office action.

Claims 1 and 19 now recite a polypeptide comprising the V domain of sRAGE or a derivative thereof capable of inhibiting the interaction between AGE and RAGE. While the definition of a derivative of soluble receptor for sRAGE (page 8, l.31 theough page 9, line 8) includes a soluble extracellular portion of the receptor and an antibody specifically capable of binding to the receptor for RAGE, claims 14 and 31 remain rejected for the reasons of record in the Office action of 6/24/99, page 3, because they are not enabled for a peptidomimetic or a polypeptide analog.

4. No claim is allowed.

5. This is a CPA of applicant's earlier Application No. 08/905,709. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eliane Lazar-Wesley, PhD, whose telephone number is (703) 305 4059. The examiner can normally be reached on Monday-Friday from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310.

Official papers filed by fax should be directed to (703) 308 4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

ELW
June 13, 2000

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER